**REMARKS**

Claims 20, 34-35, 47-49, 70-91 and 94-122 are pending in the subject application. By this amendment, applicants have canceled claims 20, 34-35, 47-49, 70-91 and 94-122 and added new claims 123-143. Therefore, claims 123-143 are now pending in this application.

Applicants have also amended the specification, *inter alia*, to include a reference to U.S. Provisional Application No. 60/101,825, filed September 25, 1998, and U.S. Provisional Application No. 60/101,693, filed September 25, 1998, as required by 35 U.S.C. §120 to claim the benefit of these provisional applications.

Support for the amendment to page 14, Table 1 may be found on page 22, lines 7-9, page 14, lines 5-15 and page 23, lines 1-30 of the subject specification. Specifically, page 22, lines 7-9 of the subject specification indicates that when a polypeptide is designated by a TV-##, the ## refers to the number of amino acids in the polypeptide, thus suggesting that the TV-## for each SEQ. ID. NO. may be discerned by counting the number of amino acids. Further proof may be found in the correlation of Table 1 on page 14, lines 5-15 of the subject specification with Table 2 on page 23, lines 1-30 of the subject specification. Both tables sequentially list polypeptides consisting of 35, 45, 56, 66, 77, 86 and 109 amino acids, which are denoted by their TV-##s in Table 2. For every TV-## listed in Table 2, the number of each type of amino acid comprising the polypeptide is equal to the number of amino acids of that type in the corresponding polypeptide listed under its SEQ. ID. NO. in Table 1. By correlating the TV-## from Table 2 with its corresponding SEQ. ID. NO. from Table 1, one of skill in

the art would readily understand that SEQ ID NO. 1 is TV-35, SEQ ID NO. 2 is TV-45, SEQ ID NO. 3 is TV-56, SEQ ID NO. 4 is TV-66, SEQ ID NO. 5 is TV-77, SEQ ID NO. 6 is TV-86 and SEQ ID NO. 7 is TV-109.

Support for the amendment to page 56, paragraphs 1-2 may be found, *inter alia*, on page 4, lines 17-20, page 15, lines 15-22 and page 46, lines 7-10 of the subject specification.

Support for new claim 123 may be found, *inter alia*, on page 6, lines 29-31, page 13, lines 25-27, page 14, lines 5-14, page 15, lines 15-18, and page 17, lines 18-32 of the subject specification. Specifically, support for a method of treating disease by the administration of a purified polypeptide of the subject invention may be found, *inter alia*, on page 6, lines 29-31, page 15, lines 15-18. Support for treating or preventing autoimmune disease in a mammal may be found, *inter alia*, on page 17, lines 18-32. Support for the purified polypeptides having the amino acid sequences SEQ ID NOS 1-7 may be found, *inter alia*, on page 13, lines 25-27 and page 14, lines 5-14.

Support for new claims 124-125 may be found, *inter alia*, on page 11, lines 10-11 of the subject specification.

Support for new claims 126-132 may be found, *inter alia*, on page 13, lines 25-26 and page 14, lines 5-14 of the subject specification.

Support for new claim 133 may be found, *inter alia*, on page 6, lines 29-31, page 7, line 21, page 13, lines 25-27, page 14, lines 5-14, page 15, lines 15-18, page 16, line 1-2 and page 17, lines 18-32 of the subject specification. Specifically, support for a

method of treating disease by the administration of a pharmaceutical composition comprising a purified polypeptide of the subject invention may be found, *inter alia*, on page 6, lines 22-25 and 29-31, page 7, line 21, page 15, lines 15-18. Support for treating or preventing autoimmune disease in a mammal may be found, *inter alia*, on page 17, lines 18-32. Support for the purified polypeptides having the amino acid sequences SEQ ID NOS 1-7 may be found, *inter alia*, on page 13, lines 25-27 and page 14, lines 5-14. Support for the pharmaceutical composition comprising a pharmaceutically acceptable carrier may be found, *inter alia*, on page 16, lines 1-2.

Support for new claim 134 may be found, *inter alia*, on page 13, lines 25-27, page 14, lines 5-23, page 17, lines 18-32 and page 18, lines 8-12 of the subject specification.

Support for new claims 135-136 may be found, *inter alia*, on page 17, lines 22-23 of the subject specification.

Support for new claim 137 may be found, *inter alia*, on page 17, lines 22-24 of the subject specification.

Support for new claims 138 and 140 may be found, *inter alia*, on page 17, lines 22-23 and 25-26 of the subject specification.

Support for new claim 139 may be found, *inter alia*, on page 17, lines 22-25 of the subject specification.

Support for new claim 141 may be found, *inter alia*, on page 17, lines 22-23 and 25-27 of the subject specification.

Support for new claim 142 may be found, *inter alia*, on page 6,

lines 22-25 and 29-31, page 7, line 21, page 15, lines 15-18, page 13, lines 25-27, page 14, lines 5-14, page 17, lines 18-21 and page 18, lines 8-10 and 14-17 of the subject specification. Specifically, support for a method of treating disease by the administration of a pharmaceutical composition comprising a purified polypeptide of the subject invention may be found, *inter alia*, on page 6, lines 22-25 and 29-31, page 7, line 21, page 15, lines 15-18. Support for treating or preventing graft versus host disease (GVHD), host versus graft disease (HVGD) or delayed-type hypersensitivity (DTH) in a mammal may be found, *inter alia*, on page 17, lines 18-21 and page 18, lines 8-10 and 14-17. Support for the purified polypeptides having the amino acid sequences SEQ ID NOS 1-7 may be found, *inter alia*, on page 13, lines 25-27 and page 14, lines 5-14.

Support for new claim 143 may be found, *inter alia*, on page 5, lines 6-7, page 9, lines 1-5 and 11-18 page 13, lines 25-27, page 14, lines 5-14, page 27, lines 4-5 and page 33, line 24 to page 34, line 22 of the subject specification. Specifically, support for a method of determining the molecular weight of glatiramer acetate may be found, *inter alia*, on page 5, lines 6-7. Support for calibrating a chromatographic apparatus that is used for molecular weight determination with the purified polypeptides of the subject invention may be found, *inter alia*, on page 9, lines 13-18. Support for determining the molecular weight of the glatiramer acetate using the calibrated chromatographic apparatus that is used for molecular weight determination may be found, *inter alia*, on page 9, lines 1-5 and 11-13, page 27, lines 4-5 and page 33, line 24 to page 34, line 22. Support for the purified polypeptides having the amino acid sequences SEQ ID NOS 1-7 may be found, *inter*

*alia*, on page 13, lines 25-27 and page 14, lines 5-14.

**Restriction**

On page 2 of the July 1, 2002 Office Action, the Examiner entered a restriction requirement between claims defining the following allegedly independent and distinct inventions:

I. Claims 20, 34-35, 47-49 and 104-122, drawn to a polypeptide or a plurality of polypeptides, a pharmaceutical composition thereof, and a kit thereof; and

II. Claims 70-91 and 94-103, drawn to a method for treating an immune disease comprising administering glatiramer acetate or a terpolymer.

In reply, applicants elect, with traverse, the invention of Group II, directed to a method for treating immune disease.

On page 3 of the July 1, 2002 Office Action, the Examiner required applicants to elect a specific polypeptide.

Initially, applicants note that substantially similar claims reciting applicants' 7 sequences have already been examined in U.S. Serial No. 09/405,743 without being restricted, so new claims 123-143 should not be subject to restriction. Nonetheless, insofar as the restriction may apply to new claims 123-143, applicants elect SEQ ID NO: 1, with traverse. Applicants note that new claims 123-143 are directed to 7 specific sequences. Applicants contend that it would not be an undue burden to examine the prior art regarding

the uses of these 7 specific sequences, particularly where the same Examiner has already conducted a prior art search for the same 7 sequences in U.S. Serial No. 09/405,743 and found the 7 sequences allowable.

On page 3 of the July 1, 2002 Office Action, the Examiner also required that applicants elect a specific type of amino acid, such as L- or D-amino acids. As mentioned above, substantially similar claims reciting applicants' 7 sequences have already been examined in U.S. Serial No. 09/405,743 without being restricted, so new claims 124 and 125 should not be subject to restriction. Insofar as this restriction may be applied to the amended claims, applicants elect with traverse L-amino acids. Applicants direct the Examiner's attention to page 11, lines 10-16 of the subject specification, which states "As is known by one of skill in the art, L-amino acids occur in most natural amino acids. However, D-amino acids are commercially available and can be substituted for some or all of the amino acids..." Since one of skill in the art knows that L-amino acids can be substituted with D-amino acids, one of skill in the art would be likely to use both L- and D-amino acids. Thus, a search of the prior art concerning the uses of applicants' 7 sequences should encompass both L- and D-amino acids.

On page 3 of the July 1, 2002 Office Action, the Examiner further required applicants to elect a specific disease. Again, applicants note that substantially similar claims reciting applicants' 7 sequences have already been examined in U.S. Serial No. 09/405,743 without being restricted, so new claims 123-141 should not be subject to restriction. Insofar as the restriction may be applied to claims 123-141, applicants elect multiple sclerosis with traverse. Applicants request that the Examiner review the example

appearing on pages 37-38 of the subject specification, in which the purified polypeptides of the subject invention are tested in an EAE system. Applicants attach as **Exhibit B** hereto a copy of Tisch et al., which specifically describes EAE as an animal model of autoimmune disease on page 438, column 1, lines 25-26. Applicants respectfully direct the Examiner's attention to MPEP §2164.02, which states "[...] if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating [...]". As Tisch et al. recognize EAE as correlating to autoimmune diseases, it should be accepted as such and all autoimmune diseases should be examined in this application.

If, however, the Examiner applies the election of species requirement to the new claims, and after examining finds the species elected by applicants to be patentable, the Examiner should proceed to examine the other species pursuant to MPEP §809.02(c).

In addition, applicants assert that claim 143, drawn to a method of determining the molecular weight of glatiramer acetate, should be examined in this application. Applicants contend that a prior art search for the use of applicants' 7 sequences in the treatment of immune diseases (Group II) would reveal other uses of the 7 sequences, such as the use for the determination of the molecular weight of glatiramer acetate. Thus, it would not be an undue burden on the Examiner to maintain claim 143 in this application. Furthermore, applicants point out that the Examiner has already examined the same 7 sequences in U.S. Serial No. 09/405,743 and found that the prior art does not teach or suggest the 7 sequences. Since the sequences were not known in the prior art, uses of the

sequences could not have been known. Therefore, it would not be an undue burden on the Examiner to maintain claim 143 in this application.

## INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following Reference Items 1-160 **(Exhibits 1-150)** which are listed again on the accompanying Form PTO-1449 **(Exhibit C)**. Applicants request that the Examiner review the references and make them of record in the subject application.

This Information Disclosure Statement is being submitted before the issuance of a first Office Action on the merits in connection with the subject application. Accordingly, no fee is required and this Information Disclosure Statement shall be considered pursuant to 37 C.F.R. §1.97(b)(3).

For the convenience of the Examiner, applicants point out that Reference Items 36, 92, 108, 126, 153 and 157 were cited in the February 7, 2000 International Search Report in the corresponding PCT International Application, and a copy of the Report is enclosed as **Exhibit D**.

Applicants also point out that several of the listed references are counterparts of each other and are cumulative. Therefore, in accordance with 37 C.F.R. § 1.98(c), a counterpart of a reference is identified after the cite to the reference, but a copy of only

one of the counterparts is being provided. Applicants will provide the Examiner with copies of any reference upon request.

1. U.S. Patent No. 3,849,550, issued November 19, 1974 (Teitelbaum, et al.) **(Exhibit 1)**;

2. U.S. Patent No. 4,339,431, issued July 13, 1982 (Gaffar) **(Exhibit 2)**;

3. U.S. Patent No. 5,204,099, issued April 20, 1993 (Barbier, et al.) **(Exhibit 3)**;

4. U.S. Patent No. 5,591,629, issued January 7, 1997 (Rodriguez et al.) **(Exhibit 4)**;

5. U.S. Patent No. 5,627,206, issued May 6, 1997 (Hupe, et al.) **(Exhibit 5)**;

6. U.S. Patent No. 5,668,117, issued September 16, 1997 (Shapiro et al.) **(Exhibit 6)**;

7. U.S. Patent No. 5,719,296, issued February 17, 1998 (Acton, III, et al.) **(Exhibit 7)**;

8. U.S. Patent No. 5,800,808, issued September 1, 1998 (Konfino, et al.) **(Exhibit 8)**;

9. U.S. Patent No. 5,858,964, issued January 12, 1999 (Aharoni, et al.) **(Exhibit 9)**;

10. U.S. Patent No. 5,981,589, issued November 9, 1999 (Konfino, et al.) **(Exhibit 10)**;

11. U.S. Patent No. 5,958,972, issued September 28, 1999 (Hupe, et al.) **(Exhibit 11)**;

12. U.S. Patent No. 6,048,898, issued April 11, 2000 (Konfino, et al.) **(Exhibit 12)**;

13. U.S. Patent No. 6,054,430, issued April 25, 2000 (Konfino, et al.) **(Exhibit 13)**;

14. U.S. Patent No. 6,214,791, issued April 10, 2001 (Arnon, et al.) **(Exhibit 14)**;

15. U.S. Patent No. 6,342,476, issued January 29, 2002 (Konfino, et al.) **(Exhibit 15)**;

16. U.S. Patent Publication No. US-2001-0055568-A1, published December 27, 2001 (Gilbert et al.) **(Exhibit 16)**;

17. U.S. Serial No. 09/359,099, filed July 22, 1999 (Strominger et al.) **(Exhibit 17)**;

18. U.S. Serial No. 09/405,743, filed September 24, 1999 (Gad et al.). Applicants point out that this reference is a counterpart of the subject application **(Exhibit 18)**;

19. U.S. Serial No. 09/816,989, filed March 23, 2001 (Gad et al.). Applicants point out that the subject application is a counterpart of U.S. Serial No. 09/405,743 (Exhibit 18);

20. U.S. Serial No. 09/875,429, filed June 5, 2001 (Yong and Chabot) **(Exhibit 19)**;

21. U.S. Serial No. 09/885,227, filed June 20, 2001 (Rodriguez and Ure) **(Exhibit 20)**;

22. PCT International Application No. PCT/US88/02139 (WO 88/10120), published December 29, 1988 (Weiner et al.) **(Exhibit 21)**;

23. PCT International Application No. PCT/US95/06551 (WO 95/31990), published November 30, 1995 (Konfino et al.). Applicants point out that this reference is a counterpart of U.S. Patents Nos. 5,800,808 (Exhibit 8) and 6,342,476 (Exhibit 15);

24. PCT International Application No. PCT/EP95/02125 (WO 95/33475), published December 14, 1995 (Kott et al.) **(Exhibit 22)**;

25. PCT International Application No. PCT/US98/00375 (WO 98/30227), published July 16, 1998 (Arnon et al.). Applicants point out that this reference is a counterpart of US Patent No. 6,214,791 (Exhibit 14);

26. PCT International Application No. PCT/US99/16617 (WO 00/05249) published February 3, 2000 (Strominger et al). Applicants point out that this reference is a counterpart of U.S. Serial No. 09/359,099 (Exhibit 17);

27. PCT International Application No. PCT/US99/16747 (WO 00/05250) published February 3, 2000 (Aharoni et al.). Applicants point out that this reference is a counterpart of the subject application;

28. PCT International Application No. PCT/US99/22402 (WO 00/18794) published April 6, 2000 (Gad, et al.). Applicants point out that this reference is a counterpart of U.S. Serial No. 09/405,743 (Exhibit 18) and U.S. Serial No. 09/816,989;

29. PCT International Application No. PCT/US99/22836 (WO 00/20010) published April 13, 2000 (Flechter, et al.) **(Exhibit 23)**;

30. PCT International Application No. PCT/US99/27107 (WO 00/27417) published May 18, 2000 (Aharoni et al.) **(Exhibit 24)**;

31. PCT International Application No. PCT/US01/05198 (WO 01/60392) published August 23, 2001 (Gilbert et al.) Applicants point out that this reference is a counterpart of U.S. Patent Publication No. US-2001-0055568-A1 (Exhibit 16);

32. PCT International Application No. PCT/US01/18248 (WO 01/93828) published December 13, 2001 (Yong and Chabot). Applicants point out that this reference is a counterpart of U.S. Serial No. 09/875,429 (Exhibit 19);

33. PCT International Application No. PCT/US01/19649 (WO 01/97846) published December 27, 2001 (Rodriguez and Ure). Applicants point out that this reference is a counterpart of U.S. Serial No. 09/885,227 (Exhibit 20);

34. European Patent Application No. 0 383 620 A2, published August 22, 1990 (Cook) **(Exhibit 25)**;

35. European Patent No. 0 359 783 B1, published November 29, 1995 (Werner, et al.);

36. Teitelbaum, et al., "Suppression of Experimental Allergic

Encephalomyelitis by a Synthetic Polypeptide", Eur. J. Immunol., 1971, 1, 242-248 **(Exhibit 26)**;

37. Teitelbaum, et al., "Suppression of Experimental Allergic Encephalomyelitis by a Synthetic Polypeptide", Israel J. Med. Sci., 1971, 7, 630-631 (Abstract) **(Exhibit 27)**;

38. Arnon, et al., "Suppression of Experimental Allergic Encephalomyelitis by a Synthetic Copolymer Immunological Cross Reactive with Basic Encephalitogen", Israel J. Med. Sci., 1972, 8, 1759-1760 **(Exhibit 28)**;

39. Teitelbaum, et al., "Protection Against Experimental Allergic Encephalomyelitis", Nature, 1972, 240, 564-566 **(Exhibit 29)**;

40. Webb, et al., "Further Studies on the Suppression of Experimental Allergic Encephalomyelitis by Synthetic Copolymer", Israel J. Med. Sci., 1972, 8, 656-657 **(Exhibit 30)**;

41. Teitelbaum, et al., "Suppression of Experimental Allergic Encephalomyelitis with Basic Polymers", Eur. J. Immunol., 1973, 3, 273-279 **(Exhibit 31)**;

42. Webb, et al., "In Vivo and in Vitro Immunological Cross-reactions between Basic Encephalitogen and Synthetic Basic Polypeptides Capable of Suppressing Experimental Allergic Encephalomyelitis", Eur. J. Immunol., 1973, 3, 279-286 **(Exhibit 32)**;

43. Teitelbaum, et al., "Dose-response Studies on Experimental Allergic Encephalomyelitis Suppression by COP-1", Israel J. Med. Sci., 1974, 10(9), 1172-1173 **(Exhibit 33)**;

44. Teitelbaum, et al., "Suppression of Experimental Allergic Encephalomyelitis in Rhesus Monkeys by a Synthetic Basic Copolymer", Clin. Immunol. Immunopath., 1974, 3, 256-262 **(Exhibit 34)**;

45. Webb, et al., "Suppression of Experimental Allergic Encephalomyelitis in Rhesus Monkeys by a Synthetic Basic Copolymer", Isr. J. Med. Sci., 1975, 11, 1388 (Abstract) **(Exhibit 35)**;

46. Webb, et al., "Molecular Requirements Involved in Suppression of EAE by Synthetic Basic Copolymers of Amino Acids", Immunochem., 1976, 13, 333-337 **(Exhibit 36)**;

47. Abramsky, et al., "Effect of a Synthetic Polypeptide (COP-1) on Patients with Multiple Sclerosis and with Acute Disseminated Encephalomyelitis", J. Neurol. Sci., 1977, 31, 433-438 **(Exhibit 37)**;

48. Teitelbaum, et al., "Suppression of Experimental Allergic Encephalomyelitis in Baboons by Cop 1", Israel J. Med. Sci., 1977, 13, 1038 (Abstract) **(Exhibit 38)**;

49. Arnon, et al., "Suppression of EAE in Baboons by a Synthetic Polymer of Amino Acids", Neurol., 1978, 28, 336 (Abstract) **(Exhibit 39)**;

50. Sela, et al., "Experimental Allergic Encephalomyelitis" in Menarini Series on Immunopathology, vol. 1, First Symposium of Organ Specific Autoimmunity", Cremona, Italy, June, 1977, (Miescher P.A. ed., Schwabe Co., Basel, 1978), 9-21 **(Exhibit 40)**;

51. Alvord, et al., "Myelin Basic Protein Treatment of Experimental Allergic Encephalomyelitis in Monkeys", Ann. Neurol., 1979, 6, 469-473 **(Exhibit 41)**;

52. Keith, et al., "The Effect of COP 1, a Synthetic Polypeptide, on Chronic Relapsing Experimental Allergic Encephalomyelitis in Guinea Pigs" J. Neurol. Sci., 1979, 42, 267-274 **(Exhibit 42)**;

53. Lando, et al., "Effect of Cyclophosphamide on Suppressor Cell Activity in Mice Unresponsive to EAE", J. Immunol., 1979, 123, 2156-2160 (Abstract) **(Exhibit 43)**;

54. Lando, et al., "Experimental Allergic Encephalomyelitis in Mice - Suppression and Prevention with COP-1", Israel J. Med. Sci., 1979, 15, 868-869 (Abstract) **(Exhibit 44)**;

55. Teitelbaum, et al., "Blocking of Sensitization to Encephalitogenic Basic Protein in Vitro by Synthetic Basic Copolymer (COP 1)" in Cell Biology and Immunology of Leukocyte Function (Academic Press, New York, 1979) 681-685 **(Exhibit 45)**;

56. Teitelbaum, "Suppression of Experimental Allergic Encephalomyelitis with a Synthetic Copolymer - Relevance to Multiple Sclerosis", in Humoral Immunity in Neurological Diseases (Karcher D., Lowenthal A. & Strosberg A.D., eds., Plenum Publishing Corp., 1979) 609-613 **(Exhibit 46)**;

57. Arnon, et al., "Desensitization of Experimental Allergic Encephalomyelitis with Synthetic Peptide Analogues" in The Suppression of Experimental Allergic Encephalomyelitis and Multiple Sclerosis (Academic Press, New York, 1980) 105-107 **(Exhibit 47)**;

58. Arnon, "A Synthetic Copolymer of Amino Acids in a Clinical Trial for MS Therapy" in Progress in Multiple Sclerosis Research (Bauer, Ritter, eds., Springer Verlag New York, 1980) 416-418 **(Exhibit 48)**;

59. Bornstein, et al., "Treatment of Multiple Sclerosis with a Synthetic Polypeptide: Preliminary Results", Ann. Neurol., 1980, 8, 117 (Abstract) **(Exhibit 49)**;

60. Bornstein, et al., "Treatment of Multiple Sclerosis with a Synthetic Polypeptide: Preliminary Results", Trans. Am. Neurol. Assoc., 1980, 105, 348-350 **(Exhibit 50)**;

61. McDermott, et al., "Antigen-induced Suppression of Experimental Allergic Neuritis in the Guinea Pig", J. Neurol. Sci., 1980, 46, 137-143 **(Exhibit 51)**;

62. Arnon, "Experimental Allergic Encephalomyelitis - Susceptibility and Suppression", Immunological Rev., 1981, 55, 5-30 **(Exhibit 52)**;

63. Bornstein, et al., "Multiple Sclerosis: Trial of a Synthetic Polypeptide", Ann. Neurol., 1982, 11, 317-319 **(Exhibit 53)**;

64. Brosnan, et al., "The Response of Normal Human Lymphocytes to Copolymer 1", J. Neuropath. Exp. Neurol., 1983, 42, 356 (Abstract) **(Exhibit 54)**;

65. Lisak, et al., "Effect of Treatment with Copolymer 1 (Cop-1) on the in Vivo and in Vitro Manifestations of Experimental Allergic Encephalomyelitis (EAE)", J. Neurol. Sci., 1983, 62, 281-293 **(Exhibit 55)**;

66. Bornstein, et al., "Clinical Trials of Copolymer 1 in Multiple Sclerosis", Ann. N.Y. Acad. Sci. (USA), 1984, 366-372 **(Exhibit 56)**;

67. Bornstein, et al., "Clinical Trials of a Synthetic Polypeptide (Copolymer 1) for the Treatment of Multiple Sclerosis" in Gonsett et al., Immunological and Clinical Aspects of Multiple Sclerosis (MTP Press, The Hague, 1984) 144-150 **(Exhibit 57)**;

68. Brosnan, et al., "Copolymer 1: Effect on Normal Human Lymphocytes", Ann. N.Y. Acad. Sci. (USA), 1984, 436, 498-499 **(Exhibit 58)**;

69. Bornstein, et al., "Multiple Sclerosis: Clinical Trials of a Synthetic Polypeptide, Copolymer 1", Neurol., 1985, 35 (Suppl. 1), 103 (Abstract) **(Exhibit 59)**;

70. Brosnan, et al., "Immunogenic Potentials of Copolymer 1 in Normal Human Lymphocytes", Neurol., 1985, 35, 1754-1759 **(Exhibit 60)**;

71. Burns, et al., "Human Cellular Immune Response in Vitro to Copolymer 1 and Myelin Basic Protein (MBP)", Neurol., 1985, 35 (Suppl. 1), 170 (Abstract) **(Exhibit 61)**;

72. Teitelbaum, et al., "Monoclonal Antibodies to Myelin Basic Protein Cross React with Synthetic EAE-suppressive Copolymer, COP 1" in Proc. 7th Eur. Immunol. Mtg., Jerusalem, September 8-13, 1985 (Abstract) **(Exhibit 62)**;

73. Thompson, "MCQ Tutor: Medical Immunology Multiple Choice Questions", Immunol. Today, 1985, 6(4), 141 **(Exhibit 63)**;

74. Burns, et al., "Human Cellular Immune Response to Copolymer 1 and Myelin Basic Protein", Neurol., 1986, 36, 92-94 **(Exhibit 64)**;

75. Bornstein, "Cop 1 May be Beneficial for Patients with Exacerbating-remitting Form of Multiple Sclerosis", Adv. Ther. (USA), 1987, 4, 206 (Abstract) **(Exhibit 65)**;

76. Bornstein, et al., "A Pilot Trial of Cop 1 in Exacerbating-

remitting Multiple Sclerosis", New Eng. J. Med., 1987, 317(7), 408-414 **(Exhibit 66)**;

77. Rolak, "Copolymer-I Therapy for Multiple Sclerosis", Clin. Neuropharmacology, 1987, 10(5), 389-396 **(Exhibit 67)**;

78. Winer, "COP 1 Therapy for Multiple Sclerosis", New Eng. J. Med., 1987, 317(7), 442-444 **(Exhibit 68)**;

79. Arnon, et al., "Suppression of Demyelinating Diseases by Synthetic Copolymers", in A Multidisciplinary Approach to Myelin Disease (G. Serlupi Crescenzi, ed., Plenum Publishing Corp., 1988) 243-250 **(Exhibit 69)**;

80. Baumhefner, et al., "Copolymer 1 as Therapy for Multiple Sclerosis: The Cons", Neurol., 1988, 38(Suppl. 2), 69-71 **(Exhibit 70)**;

81. Bornstein, et al., "Clinical Experience with COP-1 in Multiple Sclerosis", Neurol., 1988, 38(Suppl. 2), 66-69 **(Exhibit 71)**;

82. Teitelbaum, et al., "Specific Inhibition of the T-cell Response to Myelin Basic Protein by the Synthetic Copolymer Cop 1", Proc. Natl. Acad. Sci. USA, 1988, 85, 9724-9728 **(Exhibit 72)**;

83. Arnon, et al., "Suppression of Experimental Allergic Encephalomyelitis by Cop-1 - Relevance to Multiple Sclerosis", Israel J. Med. Sci., 1989, 25, 686-689 **(Exhibit 73)**;

84. Bornstein, et al., "Pilot Trial of COP-1 in Chronic Progressive Multiple Sclerosis: Preliminary Report", from The International Multiple Sclerosis Conference: An Update on Multiple Sclerosis, Roma (Italy), September 15-17, 1988, in Elsevier Science Publisher, 1989, 225-232 **(Exhibit 74)**;

85. Teitelbaum, et al., "Clinical Trial of Copolymer 1 in Multiple Sclerosis" J. Israel Med. Assoc., 1989, CXVI(9), 453-456 **(Exhibit 75)**;

86. Bornstein, et al., "Clinical Trials of Cop 1 in Multiple Sclerosis" in Handbook of Multiple Sclerosis (S.D. Cook Marcel Rekker, ed., 1990) 469-480 **(Exhibit 76)**;

87. Carter, et al., "Newer Drug Therapies for Multiple Sclerosis", Drug Therapy, 1990, 31-32, 37-39, 42-43 **(Exhibit 77)**;

88. Grgacic, et al., "Cell-mediated Immune Response to Copolymer 1 in Multiple Sclerosis Measured by the Macrophage Procoagulant Activity Assay", Int. Immunol., 1990, 2(8), 713-718 **(Exhibit 78)**;

89. Kay, et al., "The Mechanism of Action of FK 506", Transplantation Proceedings, 1990, 22(1, Suppl. 1), 96-99 **(Exhibit 79)**;

90. Lee, et al., "Peptide and Protein Drug Delivery" in Advances in Parenteral Sciences (Vincent H.L. Lee, ed., Marcel Dekker, Inc., 1990) 691-695 **(Exhibit 80)**;

91. Myers, et al., "The Peculiar Difficulties of Therapeutic Trials for Multiple Sclerosis", Neurologic Clinics, 1990, 8(1), 119-141 **(Exhibit 81)**;

92. Sela, et al., "Suppressive Activity of COP-1 in EAE and its Relevance to Multiple Sclerosis", Bull. Inst. Pasteur, 1990, 88, 303-314 **(Exhibit 82)**;

93. Starzl, Transplantation Proceedings, 1990, 22 (1, Suppl. 1), 5 **(Exhibit 83)**;

94. Wender, "Copolymer 1 (COP-1) in the Treatment of Multiple Sclerosis (letter)" Neur. Neurochir. Pol., 1990, 24, 113 **(Exhibit 84)**;

95. Bornstein, et al., "A Placebo-controlled, Double-blind, Randomized Two-center, Pilot Trial of Cop 1 in Chronic Progressive Multiple Sclerosis", Neurol., 1991, 41, 533-539 **(Exhibit 85)**;

96. Burns, et al., "Failure of Copolymer 1 to Inhibit the Human T-cell Response to Myelin Basic Protein", Neurol., 1991, 41, 1317-1319, **(Exhibit 86)**;

97. Clinical Trial Protocol No. 9001, Teva Pharmaceutical Industries, Ltd., first patient enrolled October 23, 1991 **(Exhibit 87)**;

98. Ferrara, et al., "Graft-Versus-Host Disease", New Eng. J.

Med., 1991, 324, 667-674 **(Exhibit 88)**;

99. Meiner, "COP-1 Multicenter Clinical Trial in Exacerbating-remitting Multiple-Sclerosis: One Year Follow-up", J. Neurol., 1991(Suppl. 1) (Abstract) **(Exhibit 89)**;

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